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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/742,148	12/19/2000	Roland Buelow	A-61008-1/RFT/TAL	8637

7590 09/10/2004

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/742,148	BUELOW, ROLAND	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14 and 17-19* is/are rejected.

7)☒ Claim(s) *15 and 16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/14/2004 has been entered.

Claims 13-19 are pending.

Claims 13-19 read on a compound comprising an oligopeptide of SEQ ID NO:3 and are under consideration in the instant application.

In view of the amendment, filed 07/14/2004, the following rejections remain

2. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

3. Claim 13 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 13 is indefinite and ambiguous in the recitation of: " wherein said oligopeptide includes the sequence at the amino acid positions corresponding to residues 84 to 86 of sad HLA-Bα1 domain". The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how an oligopeptide of only 6 amino acid can have amino acids 84 to 86 ?

Also the issue that recitation of HLA-Bα1 domain without providing SEQ ID NO for the protein is indefinite and ambiguous because different laboratories may have the same name for a different proteins.

Applicant's argument, filed 07/14/2004 have been fully considered, but have not been found convincing.

Applicant asserts that: claim 13 has been rephrased to expressly state the compound implicit in the prior filed claims.

Contrary to Applicant's assertion: the amended claim 13 still recited " wherein said oligopeptide includes the sequence at the amino acid positions corresponding to residues 84 to 86 of sad HLA-Bα1 domain" . The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how an oligopeptide of only 6 amino acid can have amino acids 84 to 86.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 13, 14, and 17-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a compound consisting of specific oligopeptide SEQ ID NOs 3-56 does not reasonably provide enablement for: (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 17-19. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 02/11/2004.

Applicant's arguments, filed 07/14/2004 have been fully considered, but have not been found convincing.

Applicant asserts that: (i) the Specification provided a examples of biological activities of peptide 15, 16 17 and 19 all of which contain the triad YYW and are within the scope of the claimed compound; (ii) the Specification has disclosed HLA-Bα1 domain derived oligopeptides containing the triad YYW that maintained biological activity despite significant variations in the amino or carboxy terminal sequences; (iii) a person skilled in

the art could use standard experimental techniques to determine which other embodiments comprising the recited oligopeptide.

Contrary to Applicant's assertion the issue raised by the Examiner was that Applicant only discloses an oligopeptides consisting of SEQ ID NOS: 3-56 that can modulate lymphocyte activity in the instant specification (see pages 15-18 in particular). Moreover, Applicant's recitation that peptide 15, 16 17 and 19 have biological activities supports the examiner position. It is noted that all recited peptides consists not comprises a specific SEQ ID NOs i.e. peptide 15 is a SEQ ID NO: 17, peptide 16 is a SEQ ID NO:18 etc. As was acknowledge supra, the specification is enabling for a compound consisting of specific oligopeptide of SEQ ID NO: 3-56.

Applicant has not taught how to make and use i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 that can modulate lymphocyte activity. The structural and functional characteristics of said oligopeptides are not defined in the specification and in the claims. The specification fails to provide sufficient guidance as to which core structure of SEQ ID NOs: 3-56 is essential for maintain their activity and which changes can be made in the structure of SEQ ID NOs 3-56 and still maintained the same function. Moreover, Applicant himself acknowledge that only a specific sequences including amino acids at specific position are permitted to performed the claimed modulation of lymphocyte activity (see page 10, lines 10-20 in particular). Applicant also stated that among oligopeptide comprising the recited structures only several maintained their activity and protein E, for example, has no activity at all (see page 22, lines 5-30 in paricular).

"Comprising" is considered open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 16 and 17 includes an unlimited number of amino acid sequences "comprising" an unlimited number of polypeptides. The disclosure of SEQ ID NOS: 3-56 cannot support the entire genus of *any* compound comprising an oligopeptide of at least 6 amino

acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 17-19 as part of their sequence that maintained the same function.

With regards to the issue that a person skilled in the art could use standard experimental techniques to determine which other embodiments comprising the recited oligopeptide.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Also an issue is that Applicant has not taught how to make and use a compound comprising an oligopeptide of 6 amino acids wherein amino acids 84 to 86 are YYW, as claimed in claim 13. The claim as written encompass an oligopeptide of 6 amino acid. It is unclear how one skill in the art can make an oligopeptide of only 6 amino acid that will have triad YYW at position 84 to 86 as part of their sequence?

Applicant is relying upon certain biological activities and the disclosure of a limited number of species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 17-19 encompassed by the claimed invention other than "a compound consisting of specific oligopeptide SEQ ID NOs 3-56" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determined its structural and functional properties, predictability of which fragments will retain functionality requires knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence contribute to its structure, and therefore, function. The problem of predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) *any* compound comprising an oligopeptide of at least 6 amino acids comprising a contiguous sequence of the HLA-B α1 including the triad YYW, corresponding to HLA-B α1 domain amino acids 84-86 recited in claim 13; (ii) *any* compound comprising an oligopeptide of at least 8 amino acids comprising the triad YYW and comprising a contiguous sequence of the sequence as recited in Claim 14; or (iii) *any* compounds comprising amino acid sequences recited in Claims 17-19 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

The following new ground of rejection is necessitated by the amendment filed 07/14/2004

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

6. Claim 13 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,723,128.

US'128 teaches a compound capable of modulation cytotoxic T cell comprising an oligopeptide of at least 6 amino acid, comprising a contiguous sequence of HLA-B α1 domain (see entire document, Abstract and column 4 in particular). US Patent '128 teaches that said oligopeptides includes fragment of a portion of the amino acid between position 55 and 120 of HLA-Bα1 domain (see column 2 in particular). Said compound would inherently include the sequence corresponding to residues 84 to 86 of HLA-Bα1 as claimed in claim 13.

The reference teaching anticipates the claimed invention.

7. Claims 15 and 16 are objected to in being dependent upon rejected base claim 14, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. No claim is allowed

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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